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| 10/523,353 | 03/07/2005 | Qing Yang | F-8566 | 8302 |

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| EXAMINER | |
|---|---|
| NEGIN, RUSSELL SCOTT | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/523,353 | YANG, QING | |
| | Examiner | Art Unit | |
| | Russell S. Negin | 1631 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,14-29 and 34-43* is/are rejected.

7)☒ Claim(s) *10-13 and 30-33* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 January 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/28/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Comments*

Claims 1-43 are pending and examined in the instant Office action.

### *Information Disclosure Statement*

The information disclosure statement of 28 January 2005 is considered and entered.

### *Priority*

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Australia on 30 April 2004. It is noted, however, that applicant has not filed a certified copy of the 2004902360 application as required by 35 U.S.C. 119(b).

### *Claim Objections*

Claims 10-13 and 30-33 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Int his instance, claim 10 has specific equations which are not defined or made obvious in the prior art. Claims 30-33 have specific limitations on relations between venous and arterial input functions that are not defined or made obvious in the prior art.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 14-25 and 34-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 14, it is unclear if the simulated transport function $h_s(t)$ is equivalent to the tissue transport function $h_s(t)$ in claim 4 or if it is drawn to a different function.

In claim 35, the permeability surface area product is defined in terms of variables that have not been explicitly defined in the instant claim or the claims from which claim 35 depends.

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-6, 26-29, and 36-43 are rejected under 35 U.S.C. 102(e) as being anticipated by Ostergaard [US Patent 7,069,068; issued 27 June 2006; entered national stage 15 November 2001].

Claim 1 is drawn to a method of deriving blood perfusion indices for a region of interest (ROI) of a subject.

--administering a contrast agent to the subject during a dynamic imaging scan;

--converting signal intensity data from raw images of the scan into contrast agent concentration data;

--deriving parameters from the contrast agent concentration data using at least one transport function that accounts for delay and dispersion of the contrast agent; and

--calculating the blood perfusion indices from the derived parameters.

The invention of Ostergaard describes a method for determining hemodynamic indices by the use of tomographic data. The abstract of Ostergaard explains:

> Haemodynamic indices of an organ or a part of tissue are determined from a time series of tomographic data obtained by means of Magnetic Resonance Imaging. Maps of indices are produced. Maps of indices are produced, being significant of the dynamics of the capillary tissue flow acquired during rapid bolus injection of a tracer that stays mainly intravascular.

Consequently, blood perfusion indices are identified in regions of interest of the body (i.e. preamble of instant claim 1).

The MRI imaging protocol described in column 16, line 62 to column 17, line 12 of Ostergaard describes imaging of a contrasting agent during dynamic image scanning (i.e. first step of instant claim 1).

Equation 15 of column 17 in Ostergaard converts signal intensity data from raw images to concentration data (i.e. second step of instant claim 1).

Equations 11 and 12 in column 15 of Ostergaard et al. also show how to derive parameters (i.e. the matrices in Equation 12) and calculate blood perfusion indices (i.e.

CBF in Equation 12 of Ostergaard) using a transport function (i.e. Equation 11 of Ostergaard). The numerical process of the solving of these two equations is stated in column 17, lines 50-58 of Ostergaard (i.e. third and fourth steps of claim 1).

Claim 2 is further limiting wherein the transport function represents a probability distribution function of transit times of the contrast agent through the subject. Equation 11 of in column 15 of Ostergaard represents a residence time distribution of the bolus in a given sample. In other words, Equation 11 calculates the probability a "slice" of the bolus is within a given volume after a given time. Furthermore, equation 23 in column 29, lines 30-35 of Ostergaard emphasizes the use of a probability density function in solving the above mentioned equations involving residence time distributions.

Claim 3 is further limiting comprising the step of using a first model to represent an arterial transport function through a vessel leading to the ROI.

Claim 4 is further limiting comprising a second model to represent a tissue transport function through the ROI.

Example 3 starting in column 27, line 5 of Ostergaard exemplifies modeling cerebral blood flow with the required arterial transport function listed in equations 21-22 in column 29 of Ostergaard.

Example 5 starting in column 42, line 25 of Ostergaard exemplifies modeling renal plasma flow with the required tissue transport function listed in equations 27-29 in column 45 of Ostergaard.

Claim 5 is further limiting comprising the step of selecting an arterial input function in the vessel leading to the ROI by searching pixels taken of the contrast agent concentration data.

Claim 6 is further limiting comprising the step of measuring the contrast agent concentration remaining in the ROI.

Column 27, lines 45-50 of Ostergaard details the use of the AIF and pixels taken from the contrasting agent data.

Equation 19 in column 28 details the concentration of agent as a function of time.

Claim 26 is further limiting wherein the ROI is a tissue.

Claim 27 is further limiting wherein the ROI is a pixel or plurality of pixels in a tissue.

As the title of Ostergaard suggests, the tissue of interest is blood. Column 5, lines 15-35 of Ostergaard detail that the images taken of the blood tissue within organs is pixilated.

Claim 28 is further limiting wherein the scan comprises MRI.

Claim 29 is further limited wherein the vessel is an artery.

The abstract of Ostergaard details that the scan comprises MRI.

Figure 10 of Ostergaard diagrams the modeling of the vasculature as a major, feeding artery.

Claim 36 is further limiting wherein there is a computer program means for deriving blood perfusion indices for a region of interest

Claim 37 is further limiting wherein the computer program means is further directed to retrieving raw image data from the dynamic imaging scan after a contrast agent is administered to the subject.

Claim 23 of Ostergaard recites the computer means for performing the aforementioned invention of Ostergaard.

Claim 38 is drawn to a system for performing the method of instant claim 1.

Column 5, lines 22-56 of Ostergaard detail the system for performing the method of instant claim 1.

Claim 39 is further limiting wherein the transport function represents a probability distribution function of transit times of the contrast agent through the subject. Equation 11 of in column 15 of Ostergaard represents a residence time distribution of the bolus in a given sample. In other words, Equation 11 calculated the probability a "slice" of the bolus is within a given volume after a given time. Furthermore, equation 23 in column 29, lines 30-35 of Ostergaard emphasizes the use of a probability density function in solving the above mentioned equations involving residence time distributions.

Claim 40 is further limiting comprising the step of using a first model to represent an arterial transport function through a vessel leading to the ROI.

Claim 41 is further limiting comprising a second model to represent a tissue transport function through the ROI.

Example 3 starting in column 27, line 5 of Ostergaard exemplifies modeling cerebral blood flow with the required arterial transport function listed in equations 21-22 in column 29 of Ostergaard.

Example 5 starting in column 42, line 25 of Ostergaard exemplifies modeling renal plasma flow with the required tissue transport function listed in equations 27-29 in column 45 of Ostergaard.

Claim 42 is further limiting comprising the step of selecting an arterial input function in the vessel leading to the ROI by searching pixels taken of the contrast agent concentration data.

Claim 43 is further limiting comprising the step of measuring the contrast agent concentration remaining in the ROI.

Column 27, lines 45-50 of Ostergaard details the use of the AIF and pixels taken from the contrasting agent data.

Equation 19 in column 28 details the concentration of agent as a function of time.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

35 U.S.C. 103 Rejection #1:

Claims 7-9 rejected under 35 U.S.C. 103(a) as being unpatentable over Ostergaard as applied to claims 1-6, 26-29, and 36-43 above, and further in view of Fogler [Elements of Chemical Reaction Engineering, 2nd Ed, 1992, chapter 13, section 13.4, pages 729-737].

Claims 1-6 recite a method of deriving blood perfusion indices for a region of interest, as set forth above.

Claim 7 is further limiting comprising the step of representing h(t) using a gamma variate function using the equations listed on page 3 of the instant claims.

Claim 8 is a species of the equations in instant claim 7 with some of the parameters set to zero.

Claim 9 is further limiting by showing the relevant convolution integral for determining the estimate of the arterial input function at the entry of the ROI.

Ostergaard teaches determination of blood perfusion indices for an injection of a bolus into a blood stream, as set forth above. Ostergaard further teaches a convolution integral, in Equation 19 in column 29 similar to that of instant claim 9.

However, Ostergaard does not explicitly quantify the gamma variate function as required by instant claims 7 and 8.

Fogler teaches a generic approach to teaching residence time distributions in reactors and step tracer analysis in Chapter 13. Specifically, equation 13-42 (page 731) and equation 13-50 (page 734) taken in combination teach the limitations of the equations in instant claims 7-8.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the method of determining perfusion indices of Ostergaard by use of the residence time distributions of Fogler because it is obvious to apply a known technique to a known method to yield a predictable result. In this instance, it would have been obvious to apply the known technique of residence time distribution modeling of Fogler to the blood perfusion modeling of Ostergaard where the result would have been additional modeling of blood in a physiological system. There is a reasonable expectation of success because both methods (Ostergaard and Fogler) are drawn to step tracer analyses (i.e. injecting a bolus of reactant into a flowing reactor or body and modeling its distribution over time), and Fogler gives more specific equations by which the blood perfusion studies of chemical injections could be advanced.

## ***Conclusion***

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the central PTO Fax Center. The faxing of such pages must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The Central PTO Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Negin, Ph.D., whose telephone number is (571) 272-1083. The examiner can normally be reached on Monday-Friday from 7am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Marjorie Moran, Supervisory Patent Examiner, can be reached at (571) 272-0720.

Information regarding the status of the application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information on the PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RSN
4 January 2008 1/4/08

/Marjorie A. Moran/
SPE, AU 1631
1/6/2008